assay as follows: Transfer an accurately measured representative quantity of the sample to an appropriate-sized volumetric flask. Dilute to volume with 0.1*N* hydrochloric acid to obtain a stock solution of convenient concentration containing not less than 150 micrograms of oxytetracycline per milliliter (estimated). Further dilute an aliquot of the stock solution with sterile distilled water to the reference concentration of 0.24 microgram of oxytetracycline per milliliter (estimated).

(2) *Sterility.* Proceed as directed in § 436.20 of this chapter, using the method described in paragraph (e)(1) of that section.

(3) *Pyrogens.* Proceed as directed in § 436.32(b) of this chapter, using a solution containing 5.0 milligrams of oxytetracycline per milliliter.

(4) [Reserved]

(5) *Depressor substances.* Proceed as directed in § 436.35 of this chapter.

(6) *pH.* Proceed as directed in § 436.202 of this chapter, using the undiluted solution.

[43 FR 11166, Mar. 17, 1978, as amended at 46 FR 60568, Dec. 11, 1981; 48 FR 51293, Nov. 8, 1983; 50 FR 19920, May 13, 1985]

§ 446.267 Oxytetracycline hydrochloride for injection.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Oxytetracycline hydrochloride for injection is a dry mixture of oxytetracycline hydrochloride and a suitable buffer substance. Its potency is satisfactory if it is not less than 90 percent and not more than 115 percent of the number of milligrams of oxytetracycline that it is represented to contain. It is sterile. It is nonpyrogenic. It contains no depressor substances. Its loss on drying is not more than 3.0 percent. Its pH in an aqueous solution containing 25 milligrams per milliliter is not less than 1.8 and not more than 2.8. The oxytetracycline hydrochloride used conforms to the standards prescribed by § 446.67a(a)(1), except sterility, pyrogens, and depressor substances.

(2) *Labeling.* It shall be labeled in accordance with the requirements of § 432.5 of this chapter.

(3) *Requests for certification; samples.* In addition to complying with the requirements of § 431.1 of this chapter, each such request shall contain:

(i) Results of tests and assays on:

(*a*) The oxytetracycline hydrochloride used in making the batch for potency, loss on drying, pH, absorptivity, identity, and crystallinity.

(*b*) The batch for potency, sterility, pyrogens, depressor substances, loss on drying, and pH.

(ii) Samples required:

(*a*) The oxytetracycline hydrochloride used in making the batch: 10 packages, each containing approximately 300 milligrams.

(*b*) The batch:

(*1*) For all tests except sterility: A minimum of 10 immediate containers.

(*2*) For sterility testing: 20 immediate containers, collected at regular intervals throughout each filling operation.

(b) *Tests and methods of assay*—(1) *Potency.* Proceed as directed in § 436.106 of this chapter, preparing the sample for assay as follows: Reconstitute as directed in the labeling. Then, using a suitable hypodermic needle and syringe, promptly remove all the withdrawable contents if it is represented as a single dose container; or, if the labeling specifies the amount of potency in a given volume of the resultant preparation, remove an accurately measured representative portion from the container. Dilute the sample thus obtained with sufficient 0.1*N* hydrochloric acid to obtain a stock solution of convenient concentration containing not less than 150 micrograms of oxytetracycline per milliliter (estimated). Further dilute an aliquot of the stock solution with sterile distilled water to the reference concentration of 0.24 microgram of oxytetracycline per milliliter (estimated).

(2) *Sterility.* Proceed as directed in § 436.20 of this chapter, using the method described in paragraph (e)(1) of that section, except use diluting fluid D in lieu of diluting fluid A.

(3) *Pyrogens.* Proceed as directed in 436.32(b) of this chapter, using a solution containing 5.0 milligrams per milliliter.

(4) [Reserved]

(5) *Depressor substances.* Proceed as directed in § 436.35 of this chapter,

using the diluent recommended by the manufacturer in the labeling for the drug.

(6) *Loss on drying.* Proceed as directed in § 436.200(b) of this chapter.

(7) *pH.* Proceed as directed in § 436.202 of this chapter, using an aqueous solution containing 25 milligrams per milliliter.

[43 FR 11167, Mar. 17, 1978, as amended at 46 FR 60568, Dec. 11, 1981; 50 FR 19920, May 13, 1985]

§ 446.275 Rolitetracycline injectable dosage forms.

§ 446.275a Rolitetracycline for intravenous use.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Rolitetracycline for intravenous use is a dry mixture of rolitetracycline and one or more suitable buffer substances. Its potency is satisfactory if it is not less than 90 percent and not more than 115 percent of the number of milligrams of rolitetracycline that it is represented to contain. It is sterile. It is nonpyrogenic. It contains no depressor substances. Its loss on drying is not more than 5 percent. When reconstituted as directed in the labeling, its pH is not less than 3.0 and not more than 4.5. The rolitetracycline used conforms to the standards prescribed by § 446.75a(a)(1).

(2) *Labeling.* It shall be labeled in accordance with the requirements of § 432.5 of this subchapter.

(3) *Requests for certification; samples.* In addition to complying with the requirements of § 431.1 of this subchapter, each such request shall contain:

(i) Results of tests and assays on:

(*a*) The rolitetracycline used in making the batch for potency, moisture, pH, crystallinity, absorptivity, and identity.

(*b*) The batch for potency, sterility, pyrogens, depressor substances, loss on drying, and pH.

(ii) Samples required:

(*a*) The rolitetracycline used in making the batch: 10 packages, each containing approximately 500 milligrams.

(*b*) The batch:

(*1*) For all tests except sterility: A minimum of 10 immediate containers.

(*2*) For sterility testing: 20 immediate containers, collected at regular intervals throughout each filling operation.

(b) *Tests and methods of assay*—(1) *Potency.* Proceed as directed in § 436.106 of this subchapter, preparing the sample for assay as follows: Reconstitute the sample as directed in the labeling. Using a suitable hypodermic needle and syringe, remove all of the withdrawable contents if it is represented as a single dose container; or if the labeling specifies the amount of potency in a given volume of the resultant preparation, remove an accurately measured representative portion from each container. Dilute the sample thus obtained with sufficient distilled water to obtain a stock solution of convenient concentration. Further dilute an aliquot of the stock solution with distilled water to the reference concentration of 0.24 microgram of rolitetracycline per milliliter (estimated).

(2) *Sterility.* Proceed as directed in § 436.20 of this subchapter, using the method described in paragraph (e)(1) of that section, except use diluting fluid D in lieu of diluting fluid A.

(3) *Pyrogens.* Proceed as directed in § 436.32(b) of this subchapter, using a solution containing 5.0 milligrams of rolitetracycline per milliliter.

(4) [Reserved]

(5) *Depressor substances.* Proceed as directed in § 436.35 of this subchapter.

(6) *Loss on drying.* Proceed as directed in § 436.200(b) of this chapter.

(7) *pH.* Proceed as directed in § 436.202 of this subchapter, using a solution prepared as directed in the labeling.

[39 FR 19076, May 30, 1974, as amended at 43 FR 11167, Mar. 17, 1978; 46 FR 46313, Sept. 18, 1981; 46 FR 60568, Dec. 11, 1981; 50 FR 19920, May 13, 1985]

§ 446.275b Rolitetracycline for intramuscular use.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Rolitetracycline for intramuscular use is a dry mixture of rolitetracycline and one or more suitable buffer substances and anesthetic agents. Its potency is satisfactory if it is not less than 90 percent and not more than 115 percent of the number of milligrams of rolitetracycline that it is